

PATENT

C.F.R. 1.136 (a) and enclose the required fee pursuant to 37 C.F.R. 1.17 (a)(1).

Applicants respectfully request consideration of the following amendments and remarks.

IN THE SPECIFICATION

Please **insert** the abstract attached hereto on a separate page captioned

"SUBSTITUTE ABSTRACT."

Please **delete** the sequence listing and substitute, therefore, the attached substitute

sequence listing.

Please **amend** the Brief Description of the Drawings beginning at page 11, line 23  
and ending at page 12, line 4 with the following rewritten paragraph:

**Figure 5**

*Nuclease sensitivity mapping of TNF- $\alpha$  3'UTR- $\alpha$ EP RNA*

5' End-labeled 3'UTR- $\alpha$ EP RNA was digested with T1, U2 or V1 nuclease directly to assay structure (*str*) (*c*, without nuclease) and, for T1 and U2, also after denaturation at 50°C in 7 M urea (*seq*).

Nucleotide ladder was generated by alkaline hydrolysis (OH).

Autoradiogram of sequencing gel is shown (Fig. 5A). Stem and loop regions relate to secondary structure at right, showing sites of nuclease attack, based on multiple analyses. GGGC is from plasmid. 2-APRE is the 2-AP response element (SEQ ID NO. 7) (Fig. 5B). Phylogenetic conservation of sequences is shown for *Homo sapiens* (human) (SEQ ID NO. 8), *Sus scrofa* (wild boar) (SEQ ID NO. 9),

PATENT

C1  
CON't

*Oryctolagus cuniculus* (rabbit) (SEQ ID NO. 10), *Bos taurus* (bull) (SEQ ID NO.11) and *Capra hircus* (goat) (SEQ ID NO.12) (Fig. 5C).

Please amend in the Detailed Description of Preferred Embodiments the paragraph on page 15, lines 10-19 with the following paragraph:

SEQ ID NO:1, SEQ ID NO:5, SEQ ID NO:2 and SEQ ID NO:6 are shown in the following Table 1.

Table 1

**SEQ ID NO:1 (upper strand) and SEQ ID NO:5 (lower strand)**

GAATTCAAACGGGGCTCCAGAACTCACTGGGGCTACAGCTTGATCCCTGACATCTG  
2817-----+-----+-----+-----+-----+-----+-----+-----+2876  
CTTAAGTTGACCCCGGAGGTCTTGAGTGACCCCGGATGTCGAAACTAGGGACTGTAGAC  
  
GAATCTGGAGACCAGGGAGCCTTGGTTCTGCCAGAATGCTGC  
2877-----+-----+-----+-----+-----+-----+-----+-----+2920  
CTTAGACCTCTGGTCCCTCGAACCAAGACCGGTCTTACGACG

**SEQ ID NO:2 (upper strand) and SEQ ID NO:6 (lower strand)**

TCAAACGGGGCTCCAGAACTCACTGGGGCTACAGCTTG  
2821-----+-----+-----+-----+-----+-----+-----+-----+2863  
CTTAAGTTGACCCCGGAGGTCTTGAGTGACCCCGGATGTCGA

PATENT

Please amend in the Detailed Description of Preferred Embodiments the paragraph beginning on page 23, line 26, and ending on page 24, line 9 with the following paragraph:

*N 3*  
pTNF- $\alpha$ ( $\Delta$ 3'UTR-i3EP) was constructed by joining SphI-digested pTNF- $\alpha$ ( $\Delta$ 3'UTR) DNA to the 333-bp SphI-SphI TNF- $\beta$  gene fragment described above which is comprised of 153 terminal bp of the 3'-UTR, the polyadenylation site, and downstream sequences. This plasmid was then digested with XhoI which cuts uniquely inside TNF- $\alpha$  intron 3. A 2-APRE DNA fragment abutted by XhoI restriction sites was then inserted into this site. The 2-APRE DNA fragment was obtained by polymerase chain reaction using pTNF- $\alpha$  DNA as template and two synthetic DNA primers of sequences 5'-CCGCTCGAGAATTCAAACCTGGGGCCTCC-3' (SEQ ID NO: 3) and 5'-CCGCTCGAGTGCAGCATTCTGGCCAGAAC-3' (SEQ ID NO:4) as 5' and 3' primers, respectively; the DNA product was digested with XhoI before ligation. Orientation of the 2-APRE insert in pTNF- $\alpha$ ( $\Delta$ 3'UTR-i3EP) was determined by analysis of DNA fragments generated upon PvuII/PstI digestion.

#### REMARKS

In response to the Notice of Incomplete Reply mailed on June 29, 2001, Applicants submit the following amendment and remarks. Applicant submit herewith an Abstract of the technical disclosure. Applicants also submit herewith a substitute Sequence Listing in computer and paper form in accordance with 37 C.F.R. §1.821-